IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	Thomas H. Barrows		
Application No.:	09/890,888	Art Unit:	1615
Filed:	August 7, 2001	Examiner:	Isis Ghali

For: FILAMENTARY MEANS FOR INTRODUCING AGENTS INTO TISSUE OF A LIVING HOST

DECLARATION UNDER 37 C.F.R. 1.132

Assistant Commissioner of Patents
Washington, D.C. 20231

Sir:

I, Thomas H. Barrows, declare as follows:

1. I have personal knowledge of the following facts and I make this declaration in support of the prosecution of U.S. Patent Application Serial No. 09/890,888 before the United States Patent and Trademark Office.

2. I am currently employed as Director of Product Development at Aderans Research Institute, a position I have held since 2002. Prior to that I was employed as Vice President of Research & Development at BioAmide, Inc.

3. My curriculum vitae is attached as Appendix A.

4. I am the inventor of the subject matter of the above-identified application and I am familiar with the art and with the prosecution history of this application.

5. I have reviewed the pending Office Action as well as the claims amended in accordance with the Amendment and Request for Continued Examination filed herewith. In particular, the Examiner asserts that U.S. Patent No. 5,486,593 to Tang et al. ("Tang") teaches fibers that can be solid (Col. 6, line 57) and coated with other polymers (Col. 7, line 36) and conductive agents (Col. 19, line 1). In the Advisory Action, the Examiner concludes

that no superior or unexpected results of record show the criticality of the core made of metal or metal alloy.

6. Tang discloses bioabsorbable polymers on devices (e.g. Col. 5, lines 49-51) made of metals (e.g. Col. 19, lines 40-42). But none of these metal objects were metal wire, needles, or filaments. In fact, Tang's bioabsorbable polymer coatings were used only on woven or knitted fibers, and were used for the purpose of sealing non-bioabsorbable vascular grafts against fluid leaks during surgery. Such vascular grafts are constructed from synthetic polymer fibers and not from metal filaments. Moreover, the use of metal filaments or, for that matter, any material which might damage tissue would most certainly not be within the disclosure or contemplation of Tang.

7. The present invention, by contrast, uses metal filaments coated with porous bioabsorbable polymers for the purpose of delivering agents, such as, but not limited to, hair follicles, hair follicle progenitor cells, and other living cells, into the tissue of the recipient.

8. The filament of the presently claimed invention is a metal or metal alloy core coated with a porous polymer sheath. In order to generate the interconnecting pores of the claimed filament, the heat applied to the coated filament must penetrate the filament quickly. The claimed metal or metal alloy core, unlike a nonmetallic core, conducts heat rapidly into the center of the filament during thermal activation of the blowing agent. The end result is a coating reticulated with interconnecting pores as desired. Put otherwise the kind of materials suggested by Tang would not and could not be used to create the porous coating of the present invention, because the materials suggested by Tang, i.e. ones which cause no tissue or organ trauma, are not sufficiently thermally conductive to be used in this invention.

9. Morevoer, the exceptional strength and toughness of metal as a core material in comparison to other materials is critically important, especially in this case where the core is a very fine diameter filament, because the filament must be capable of easily penetrating the skin. As noted, Tang's applications necessarily require minimization of tissue trauma.

10. Further, in the present invention, the core is desired to be removed from the coating, either before or after the product is implanted into the living tissue. If the core filament is metal, there is a high degree of certainty that the removal process will be successful. If any other material is used, there is a risk that the filament will break under tension, making complete removal of any broken fragments difficult and impractical. The

presence of non-bioabsorbable debris in the porous bioabsorbable polymer scaffold implantation site is not desirable.

11. I hereby declare that all statements made herein of my own knowledge are believed to be true, and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Dated this 29 day of DEC., 2003.

Thomas H. Barrows, Ph.D.
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THOMAS H. BARROWS
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SUMMARY: Biomedical materials research, supervision, bioabsorbable polymers, product development of surgical devices and implants.

EXPERIENCE:

2002-Present Aderans Research Institute, Atlanta, GA

DIRECTOR of PRODUCT DEVELOPMENT

1999-2002 BioAmide, Inc., Atlanta, GA

VICE PRESIDENT, R&D

- Initiated a project on the development of implants for tissue-engineered hair.
- Set-up a cell culture laboratory at Emtech Biotechnology, Inc. and hired a cell-biologist to perform hair follicle induction research.
- Established a Scientific Advisory Board including experts in dermatologic surgery, pathology, and research.
- Obtained IRB approval and conducted a human clinical investigation.
- Achieved the first documented clinical demonstration of follicle neogenesis and hair grow *via* implantation of cultured cells on a bioabsorbable polymer scaffold (*i.e.* tissue-engineered hair).

1999-2000 Georgia Tech/Emory Center for the Engineering of Living Tissues, Atlanta, GA

AFFILIATE

- Collaborated with Prof. Robert Guldberg and graduate student Angela Lin on the development and evaluation of high-strength scaffolds for tissue engineered bone.
- Managed a project on bioabsorbable fiber-reinforced composite pin manufacture and performance testing at Georgia Tech (with Prof. Guldberg and Angela Lin) and the University of Tennessee, Knoxville (with Prof. Spruiell and Regina Holmes).

1996-1999 Focal, Inc., Lexington, MA

PRINCIPAL SCIENTIST

- Supervised the Materials Research Team leading to the synthesis, scale-up, pre-clinical, and clinical development of FocalSeal-S™ for use in neurosurgery to prevent cerebrospinal fluid leaks and subsequent infections and meningitis.
- Direct responsibility for supervision of four Ph.D. chemists and two B.S. degree chemists.

1985-1996 Life Sciences Sector Laboratory/3M, St. Paul, MN

SENIOR RESEARCH SPECIALIST

- Invented and developed a new semi-synthetic tissue sealant for use in lung surgery that was successfully evaluated in pre-clinical and clinical studies for safety and efficacy.

- Perfected and scaled-up monomer and polymer syntheses and purification procedures under GMP at pilot plant facilities in the US and France.

1978-1985 Life Sciences Sector Research Laboratory/3M, St. Paul, MN

RESEARCH SPECIALIST

- Conducted basic research in the metabolic fate of hydrolyzable polymers using carbon-14 labeled monomers.
- Invented a new class of bioabsorbable poly(ester-amides). Designed specific polymer structures for high performance fiber applications including absorbable sutures and ligament reconstruction implants.
- Identified and developed new product opportunities in the fields of peripheral nerve repair, fracture fixation and bone remodeling, drug delivery, skin stapling, and tissue adhesives.

1974-1978 Central Research Laboratories/3M, St. Paul, MN

SENIOR RESEARCH CHEMIST

- Synthesized polymers for tissue compatibility, bioabsorbability, tissue sealant, and drug delivery studies.
- Performed analyses of bioabsorbable fiber performance characteristics using accelerated *in vitro* hydrolysis conditions.
- Conducted research on blown microfiber production of bioabsorbable polymers.

EDUCATION:

1974 Ph.D. Organic Chemistry, The Pennsylvania State University, University Park, PA

1969 B.S. Chemistry, University of Georgia, Athens, GA

1965 Sandy Springs High School, Atlanta, GA

PROFESSIONAL SOCIETIES:

The American Chemical Society
ACS Polymer Division
The Society for Biomaterials

HONORS: Fellow of the American Institute for Medical and Biological Engineering (AIMBE), Class of 1999.

Various awards bestowed by 3M including: The Circle of Technical Excellence Award, The Genesis Research Grant Award, and the Corporate Challenge '81 Award.

PATENTS:

T.H. Barrows, "Bioabsorbable Fibers and Reinforced Composites Produced Therefrom", U.S. Patent 6,511,748, January 28, 2003.

T.H. Barrows, "Device of Bioabsorbable Triglycolic Acid Poly(ester-amide)s, and Methods of Making the Same", U.S. Patent 6,365,172, April 2, 2002.

T.H. Barrows, "Hair Follicle Neogenesis by Injection of Follicle Progenitor Cells", International Patent WO 02/060396 A2, August 8, 2002.

T.H. Barrows, "Scaffolds for Tissue Engineered Hair", International Patent WO 02/15952 A1, February 28, 2002.

T.H. Barrows, "Bioabsorbable Triglycolic Acid Poly(ester-amide)s", U.S. Patent 6,120,788, September 19, 2000.

T.H. Barrows, "Filamentary Means for Introducing Agents into the Tissue of a Living Body", International Patent WO 00/45736, August 10, 2000.

T.H. Barrows, M.T. Truong, and P.R. Suszko, "Biocompatible Porous Matrix of Bioabsorable Material", U.S. Patent 5,856,367, January 5, 1999.

T.H. Barrows, T.W. Lewis, and M.T. Truong, "Adhesive Sealant Composition", U.S. Patent 5,583,114, December 10, 1996.

T.H. Barrows, M.T. Truong, and P.R. Suszko, "Biocompatible Porous Matrix of Bioabsorbable Material", U.S. Patent 5,502,092, March 26, 1996.

T.H. Barrows, M.T. Truong, P.R. Suszko, and D.W. Stegink, "Process for Increasing Stability of Poly (ester-amides)", U.S. Patent 5,286,837, February 15, 1994.

T.H. Barrows and M.T. Truong, "Bioabsorbable Poly(ester-amides) and method for Making Same", International Patent WO 93/13814, July 22, 1993.

T.H. Barrows, "Semiabsorbable Bone Plate Spacer", U.S. Patent 5, 013,315, May 7, 1991.

T.H. Barrows, "Absorbable Nerve Repair Device and Method", U.S. Patent 4,883,618, November 28, 1989.

T.H. Barrows and H.E. Froehlich, "Surgical Staple", U.S. Patent 4,719,917, January 19, 1988.

T.H. Barrows, "Absorbable Nerve Repair Device and Method", U.S. Patent 4,669,474, June 2, 1987.

T.H. Barrows, "Absorbable Sutureless Nerve Repair Device", U.S. Patent 4,534,349, August 13, 1985.

T.H. Barrows, "Process for Preparing Synthetic Absorbable Poly(ester-amides)", U.S. Patent 4,529,792, July 16, 1985.

T.H. Barrows, "Polymeric Acid Contraceptive Devices and Method", U.S. Patent 4,360,013, November 23, 1982.

T.H. Barrows, "Synthetic Absorbable Surgical Devices of Poly(ester-amides)", U.S. Patent 4,343, 931, August 10, 1982.

PUBLICATIONS:

A.S. Lin, T.H. Barrows, S.H. Cartmell, and R.E. Guldberg, "Microarchitectural and mechanical characterization of oriented porous polymer scaffolds", *Biomaterials,* **24**(3), 481-9 (2003).

T.H. Barrows, S.A. Cochran, E.I. Griffin, and A.R. Solomon, "Tissue Engineered Human Hair: Preliminary Clinical Results", *TE2002: International Workshop on Tissue Engineering*, St. Gallen, Switzerland, 24-27 February, 2002.

R.N. Holmes, J.E. Spruiell, T.H. Barrows, A.S.P. Lin and R.E. Guldberg, "Core/Sheath Polylactide Fiber-Reinforced Composites", *Trans. Soc. Biomater.*, **24**, 27 (2001).

A.S.P. Lin, T.H. Barrows, S.H. Cartmell and R.E. Guldberg, "Manufacture and Characterization of 3D Porous Scaffolds for Bone Tissue Engineering", *Trans. Soc. Biomater.*, **24**, 286 (2001).

A. Coury, T. Barrows, *et al.*, "Development of Synthetic Coatings for Textile Vascular Prostheses", *Trans. Sixth World Biomater. Cong.*, 1497, (2000).

B.C. Poff, D. Warnock, S. Barman, J. Rajaratnam, J. Terrazzano, E. Drake, T. Barrows, and A.J. Coury, "Chronic Biocompatibility of a Hydrogel Dural Sealant in the Rat Brain", *Trans. Soc. Biomater.*, **22**,42 (1999).

A.J. Coury, S.P. Barman, N. Hoffman, T.H. Barrows, and B. Poff, "Development of a Synthetic Absorbable Tissue Sealant: Preclinical Studies", *Proceedings, 4th NJ Symposium on Biomaterials and Medical Devices*, Rutgers University, New Brunswick , NJ, Nov., 1997.

T.H. Barrows, M.T. Truong, T.W. Lewis, D.M. Grussing, K.H. Kato, J.E. Gysbers, and E.G. Lamprecht, "Evaluation of a New Tissue Sealant Material: Serum Albumin Crosslinked *In Vivo* with Polyethylene Glycol" *Trans. Fifth World Biomater. Cong.*, **1**,8, (1996).

M.T. Truong, T.H. Barrows, and T.J. Wilson, "*In Vitro* Analysis of Mechanical Properties of a New Tissue Sealant Material: Polyethylene Glycol Crosslinked Serum Albumin" *Trans. Fifth World Biomater. Cong.*, **2**,73, (1996).

S. Gogolewski, P. Michel, and T.H. Barrows, "Sterility, Molecular and Mechanical Properties of Heat-Treated Resorbable Poly(Ester-Amides). PEA 10.2 and PEA 10.6", *Trans. Fifth World Biomater. Cong.*, **2**, 700, (1996).

M.T. Truong, T.H. Barrows, H.P. Goldmann, R. Althaus, and K.H. Fullgrabe, "*In Vitro* Conditions for Accelerated Hydrolysis of Bioabsorbable Fibers", *Trans. Soc. Biomater.*, **18**, 436 (1995).

T.H. Barrows, "Bioabsorbable Poly(ester-amides)", in "Designed to Degrade Biomedical Polymers", S.W. Shalaby, ed., Chapter 4, p. 97-116, Carl Hanser Verlag Publisher, 1994.

T.H. Barrows, M.T. Truong, P.R. Johnson, and M.A. Havens, "*In Vitro* Comparison of the Hydrolysis of Polylactic Acid and Poly(ester-amide) Fibers", *Trans. Fourth World Biomater. Congress*, **15**, 249 (1992).

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T.H. Barrows, "Synthetic Bioabsorbable Polymers", in "High Performance Biomaterials, a comprehensive guide to medical and pharmaceutical applications", M. Szycher, ed., Technomic. Lancaster, PA, Chapter 17, p. 243-257, 1991.

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Monomers and Polymers *In Vivo* using Radiolabeled Homologs", in Progress in Biomedical Polymers, C.G. Gebelein and R.L. Dunn. Eds., Plenum Press, New York, p. 263-282, 1990.

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T.H. Barrows, G.J. Quarfoth, P.E. Blegen, and R .L. McQuinn, "Comparison of Bioabsorbable Poly(ester-amide) Monomers and Polymers *In Vivo* using Radiolabeled Homologs", *Poly. Mater. Sci. Eng.*, **59**, (1988).

C.P. Tountas, R.A. Bergman, T.H. Barrows, *et al.*, "Peripheral Nerve Repair: tubulization vs. Suture, a 12 month primate study", American Society for Surgery of the Hand, 42nd Annual Meeting, San Antonio, TX, September 1987.

T.H. Barrows, J.D. Johnson, S.J. Gibson, and D.M. Grussing, "The Design and Synthesis of Bioabsorbable Poly(ester-amides)", in "Polymers in Medicine II", vol. **3**, E. Chiellini, ed., Plenum Press, New York, p. 85-90, 1986.

T.H. Barrows, "Degradable Implant Materials: A Review of Synthetic Absorbable Polymers and their Applications", *Clinical Materials*, **1**, 233-257 (1986).

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T.H. Barrows, D.M. Grussing, and M.A. Havens, "Comparison of Tensile and Knotted Strength Retention of Synthetic Absorbable Sutures *In Vivo*", *Trans. Soc. Biomater.*, **8**, 143 (1985).

T.H. Barrows, S.J. Gibson, and J.D. Johnson, "Poly(ester-amides): *In Vivo* Analysis of Degradation and Metabolism using Radiolabeled Polymers", *Trans. Soc. Biomater.*, **7**, 210 (1984).

T.H. Barrows, D.M. Grussing, and D.W. Hegdahl, "Poly(ester-amides): A New Class of Synthetic Absorbable Polymers", *Trans. Soc. Biomater.*, **6**, 109 (1983).

T.H. Barrows, P.R. Farina, R.L. Chrzanowski, *et al.*, "Studies on Models for Tetrahydrofolic Acid: Reactions and Mechanisms of Tetrahydroquinoxaline Derivatives at the Formaldehyde Level of Oxidation", *J. Amer. Chem. Soc.*, **98**, 3678 (1976).

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INVITED LECTURES:

"Bioabsorbable Hydrogel Tissue Sealants", Seminar, Cornell University, Ithaca, NY, November 18, 1997.

"Bioabsorbable Tissue Sealants", Clemson University Medical Textiles and Biomedical Polymers and Materials Conference, Greenville, SC, September 11-12, 1996.

"Trends in the Synthesis of Bioabsorbable Polymers". This lecture, delivered at the following locations, has been revised and updated with each presentation to cover recent developments.

Technical Workshop Number 14, The Society for Biomaterials 21st Annual Meeting, San Francisco, CA, March 18, 1995.

Clemson University Medical Textiles and Biomedical Polymers and Materials Conference, Greenville, SC, September 6-7, 1995.

Biomaterials & Medical Devices for Human Body Repair Lecture Series, Cornell University, Ithaca, NY, April 5, 1994.

Biodegradable Implant Materials Workshop, 10th European Conference on Biomaterials, Davos, Switzerland, September 8-11, 1993.